

SEP 30 2002
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF

CHATFIELD

Atty. Ref.: 117-320

SEP 03 2002

Serial No.: 09/646,925

Group Art Unit: 1645 TECH CENTER 1600/2900

Filed: January 31, 2001

Examiner: Ford, V.

For: BACTERIA ATTENUATED BY A NON-REVERTING MUTATION IN EACH
OF THE AROC, OMPF AND OMPC GENES, USEFUL AS VACCINES

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September 30, 2002

RESPONSE

Hon. Commissioner of Patents
and Trademarks
Washington, DC 20231

Sir:

This is in response to the Examiner's requirement for restriction, set forth in the Office Action dated June 28, 2002, the period for response having been extended up to September 28, 2002, by submission of the required petition and fee herewith. Applicants elect, with traverse, the subject matter of Group I (claims 1-11 and 13) for prosecution in this application.

Contrary to the Examiner's assertions, all four Groups are linked by a single general inventive concept in accordance with Rules 13.1 and 13.2 PCT. According to those Rules, unity of invention is deemed to exist where the claims share "special technical features". Special

technical features are defined as "those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art".

All the claims share the special technical feature of a bacterium attenuated by a mutation in each of the *aroC* gene, the *ompF* and the *ompC* gene. Such bacteria make a contribution over the art; in fact, they are novel over the art, as recognized in the international preliminary examination report.

The reason put forward by the Examiner for the restriction requirement is that the subject matter of Group I (a bacterium attenuated by non-reverting mutations in *aroC*, *ompF* and *ompC*) lacks novelty and therefore the subject matter of that Group cannot be used to unify the four Groups into a single Group. However, as indicated above, the subject matter of Group I does not lack novelty.

Chatfield et al discloses a bacterial cell attenuated by mutations in both *ompC* and *ompF*. Dougan et al discloses a bacterial cell attenuated by a mutation in *aroC*. Neither reference discloses a bacterial cell attenuated by mutations in all three of *ompC*, *ompF* and *aroC*.

The Examiner appears to confuse the issues of novelty and obviousness. For example, the Examiner contends that

it "would have been obvious at the time the invention was made to add the *aroC* mutants as taught by Dougan et al to the *ompC* and *ompF* mutants of Chatfield et al because Dougan et al teach that mutations in *aroC* genes were highly attenuated after intravenous inoculation". Clearly, this comment goes to the question of obviousness not novelty.

In any event, the subject matter of Group I would not have been obvious because the claimed bacteria are surprisingly immunogenic. As evidence of this surprising immunogenicity, enclosed are two reports of clinical studies. (The table of contents is missing from the report of the first study but all the substantive information is present.)

In both studies, two strains of bacteria were tested, strain "PTL-ETEC-002" and strain "PTL-ETEC-003". Strain PTL-ETEC-002 is attenuated by mutations in the *ompR* and *aroC* genes, and is not a bacterium in accordance with the claimed invention. PTL-ETEC-003 is attenuated by mutations in *aroC*, *ompC* and *ompF* and is a bacterium in accordance with the claimed invention.

The summary conclusion from the first study was that both the *aroC ompR* and *aroC ompC ompF* mutants were safe and immunogenic. The enlarged second study, designed specifically to detect differences between the two strains,

showed the *aroC ompC ompF* strain to be superior. Attention is directed to the "Discussion and Overall Conclusions" section on page 41 of the second study, where it is stated that:

"The PTL-ETEC-003 construct was superior to the PTL-ETEC-002 construct in its ability to induce both mucosal and systemic immune responses to CFA/II. PTL-ETEC-003 also exhibited a more sustained intestinal colonization than PTL-ETEC-002."

In view of the above, the Examiner is requested to reconsider the requirement for restriction. It is believed that having done so, the Examiner will find it appropriate to rejoin the subject matter of all of the 4 Groups.

Respectfully submitted,

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